

WHAT IS CLAIMED IS:

1. A composition comprising a carrier and particulates comprising a compressed mixture of an active agent and an agent exhibiting a characteristic of low solubility in water, the particulates being dispersed within
5 the carrier.
2. The composition of claim 1 wherein the agent exhibiting the characteristic of low solubility in water is hydrophobic and the carrier is a biocompatible gel.
10
3. The composition of claim 1 wherein the hydrophobic agent is selected from the group consisting of pharmaceutically acceptable oil, fats, fatty acids, fatty acid esters, waxes and mixtures and derivatives thereof that exhibit the hydrophobic characteristic.
15
4. The composition of claim 3 wherein the hydrophobic agent is selected from the group consisting of C₁₆ – C₂₄ fatty acids, esters and pharmaceutically-acceptable salts thereof, and mixtures of the foregoing.
- 20 5. The composition of claim 4 wherein the hydrophobic agent comprises a mixture of stearic acid and palmitic acid.
6. The composition of claim 5 wherein the stearic acid and the palmitic acid together constitute at least 90% by weight of the fatty acids of the
25 hydrophobic agent and the stearic acid constitutes at least 40% by weight of the fatty acids of the hydrophobic agent.
7. The composition of claim 6 wherein the stearic acid and the palmitic acid together constitute at least 96% by weight of the fatty acids of the

hydrophobic agent and the stearic acid constitutes at least 90% by weight of the fatty acids of the hydrophobic agent.

8. The composition of claim 1 wherein the particulates comprise a
5 powder.

9. The composition of claim 1 wherein the powder has a particle size such that 90% passes through a 50 mesh screen and are retained on a 400 mesh screen.

10. The composition of claim 1 wherein the active agent is water soluble.

11. The composition of claim 10 wherein the active agent is selected from the group consisting of DNA, cDNA, proteins, peptides and fragments and
15 derivatives thereof.

12. The composition of claim 10 wherein the carrier comprises a polymer selected from the group consisting of polylactic acid, polyglycolic acid and poly(lactide-co-glycolic) acid and a solvent comprising an alkyl or aralkyl
20 ester of benzoic acid.

13. The composition of claim 12 wherein the active agent is selected from the group consisting of human growth hormone, alpha-, beta- or gamma-interferon, erythropoietin, glugacon, calcitonin, heparin, interleukin-1,
25 interleukin-2, Factor VIII, Factor IX, luteinizing hormone, relaxin, follicle-stimulating hormone, atrial natriuretic factor and filgrastim.

14. The composition of claim 13 wherein the polymer is poly(lactide-co-glycolic) acid and the solvent is benzyl benzoate.

15. The composition of claim 14 wherein the polymer is poly(lactide-co-glycolic) acid and the solvent is ethyl benzoate.

5 16. A composition comprising: (a) a bioerodible gel comprising a polymer selected from the group consisting of polylactic acid, polyglycolic acid, and poly(lactide-co-glycolic) acid; (b) a solvent selected from the group consisting of an alkyl or aralkyl ester of benzoic acid; and (c) particulates dispersed within the gel, said particulates comprising a compressed mixture of an active
10 agent and an agent exhibiting a characteristic of low solubility in water selected from the group consisting of pharmaceutically acceptable oils, fats, fatty acids, fatty acid esters, waxes, derivatives thereof, and mixtures of the foregoing.

15 17. The composition of claim 16 wherein the agent exhibiting the characteristic of low solubility in water is hydrophobic.

18. The composition of claim 17 wherein the hydrophobic agent is selected from the group consisting of C₁₆- C₂₄ fatty acids, esters and pharmaceutically-
20 acceptable salts thereof, and mixtures of the foregoing.

19. The composition of claim 18 wherein the hydrophobic agent comprises a mixture of stearic acid and palmitic acid.

25 20. The composition of claim 19 wherein the stearic acid and the palmitic acid together constitute at least 90% by weight of the fatty acids of the hydrophobic agent and the stearic acid constitutes at least 40% by weight of the fatty acids of the hydrophobic agent.

21. The composition of claim 20 wherein the stearic acid and the palmitic acid together constitute at least 96% by weight of the fatty acids of the hydrophobic agent and the stearic acid constitutes at least 90% by weight of the fatty acids of the hydrophobic agent.

5

22. The composition of claim 21 wherein the particulates comprise a powder.

23. The composition of claim 22 wherein the powder has a mean particle size of about 30 microns to about 500 microns.

10

24. The composition of claim 23 wherein the active agent is water soluble.

25. The composition of claim 24 wherein the active agent is selected from the group consisting of DNA, cDNA, proteins, peptides and fragments and derivatives thereof.

15

26. The composition of claim 24 wherein the gel comprises poly(lactide-co-glycolic) acid.

20

27. The composition of claim 24 wherein the active agent is selected from the group consisting of human growth hormone, alpha-, beta- or gamma-interferon, erythropoietin, glugacon, calcitonin, heparin, interleukin-1, interleukin-2, Factor VIII, Factor IX, luteinizing hormone, relaxin, follicle-stimulating hormone, atrial natriuretic factor and filgrastim.

25

28. The composition of claim 27 wherein the solvent is benzyl benzoate and the active agent is human growth hormone.

29. The composition of claim 27 wherein the solvent is ethyl benzoate and the active agent is human growth hormone.

30. A process for the preparation of an implantable composition
5 comprising a bioerodible carrier having dispersed therein an active agent that comprises forming a compressed body of a mixture of the active agent and an agent exhibiting a characteristic of low solubility in water, crushing the body to form compressed particulates of the mixture of the active agent and the agent exhibiting a characteristic of low solubility in water, and dispersing
10 the compressed particulates throughout the carrier.

31. The process of claim 30 wherein the active agent is water soluble and the agent exhibiting a characteristic of low solubility in water is hydrophobic.

15 32. The process of claim 31 wherein the active agent is selected from the group consisting of protein and polypeptide and the hydrophobic agent is selected from the group consisting of stearic acid, palmitic acid and myristic acid.

20 33. The process of claim 32 wherein the protein is human growth hormone and the hydrophobic agent is stearic acid.

34. The process of claim 31 wherein the active agent is selected from the group consisting of cDNA, DNA, proteins, peptides and fragments and
25 derivatives thereof.

35. The process of claim 31 wherein the active agent is selected from the group consisting of human growth hormone, alpha-, beta- or gamma-interferon, erythropoietin, glugacon, calcitonin, heparin, interleukin-1,

ARC 2882 R1

56

interleukin-2, Factor VIII, Factor IX, luteinizing hormone, relaxin, follicle-stimulating hormone, atrial natriuretic factor and filgrastim.